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FUNGOUS GROWTHS IN SOLUTIONS FOR HYPODERMIC MEDICATION,

AND

THEIR PREVENTION BY SALICYLIC ACID.

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JOSEPH G. RICHARDSON, M.D.,

ATTENDING PHYSICIAN TO THE PRESBYTERIAN HOSPITAL, PHILADELPHIA.

EXTRACTED FROM THE TRANSACTIONS OF THE

INTERNATIONAL MEDICAL CONGRESS,

PHILADELPHIA, SEPTEMBER, 1876.

PHILADELPHIA:

1877.

Extracted from the Transactions of the International Medical Congress, Philadelphia, September, 1876.

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Among the minor inconveniences of medical practice, few are more annoying to the careful physician than a failure to afford the hoped or prayed-for relief from pain, by the subcutaneous injection of morphia. I therefore venture to occupy a few minutes of the time of the Section with a brief account of a new method for preventing diminution in the strength of morphia solutions, in so far as it is due to the common cause of such deterioration, namely, the formation in the fluid of fungous growths, which necessarily develop at the expense of the contained solid ingredients.

If we examine under a microscope of high power one of the white flocculent masses which appear after a week or two of warm weather in our ordinary Magendie's solution of morphia, we will commonly find it made up of an immense number of branching threads, on an average about $\frac{1}{5000}$ of an inch in diameter, often distinctly septate, and probably recognizable as the mycelial condition of one of the genera of the Mucorini or siphonaceous plants.

Complete identification of the exact species is only possible, even for the professed mycologist, by investigation of its aerial fructification. We, however, often find, as it develops entirely beneath the fluid, an evident attempt towards the formation of some sort of reproductive body, and in many cases are to be seen in active motion, near the filaments, spore-like bodies, analogous to the antherozoids of the unmistakable algæ and fungi, which have doubtless escaped from broken fragments of the aquatic mycelial threads.

The atoxic quality of salicylic acid, as demonstrated by the moderate and even large doses administered in thousands of cases of acute rheumatism, etc., suggests at once its employment for the purpose of preventing the growth of these fungi; and I think it quite probable that it has already been so used by others of my fellow-practitioners as well as by myself. No exact observations upon this subject have, however, I believe, as yet been published, at least in our own country.

In order to determine the precise amount of this antiphytic agent required to produce the desired effect, I prepared on the first of August last, now five weeks since, one dozen two drachm vials, each containing one fluidrachm of a solution of acetate of morphia (gr. xvj to f℥j), such as is usually employed for hypodermic medication. These samples were num-

bered from 1 to 12, and after the acetate, except impurities, had been dissolved by the aid of a small quantity of acetic acid, I added to Nos. 2 and 4 each one-sixteenth of a grain of salicylic acid, to Nos. 6 and 8 each one-eighth of a grain of the same substance, and to Nos. 10 and 12 each one-quarter of a grain of the like material. Nos. 1, 3, 5, 7, 9, and 11 were left unmixed with other ingredients, and all were corked tightly and equally exposed to the light, and to the unusually elevated temperature of our Centennial summer. At the end of one week, small whitish flocculi, evidently composed of filamentous tufts, were visible in the bottles the contents of which were unmixed with salicylic acid, and similar minute specks, in much less quantity, had made their appearance in Nos. 2 and 4, which contained each one-sixteenth of a grain of salicylic acid.

Under the microscope, specimens of these tufts were seen to be made up of mycelial threads, probably of some species of physomycetous fungi, such as I have already described. At the present time, after five weeks have elapsed, those vials which were not protected by salicylic acid present every one large masses of fungous growth, as each member of the Section may see for himself by inspecting them upon the table. Nos. 2 and 4, in each of which it will be remembered that one-sixteenth of a grain of the acid was dissolved, display small tufts of mycelial threads. No. 8 shows a mere trace of fungous growth, whilst Nos. 6, 10, and 12 exhibit to the naked eye (as they do also under a one-fifth objective) no indication of living fungi in the slight deposit of brownish impurities let fall at the bottom of the glass.

In specimens of similar morphia solution, containing one-eighth of a grain of salicylic acid to the fluidrachm, carried in the hypodermic syringe case, and used from time to time in my daily practice during three months of cooler spring weather, no flocculi of living fungi were discoverable with the naked eye or under the microscope. Further, no unusual effects of any kind were observable in patients, some of whom received as much as ℿviij at a dose. Injections made into my own arms for the purpose of testing the fluids in Nos. 10 and 12, produced but little smarting sensation, and afforded the ordinary anodyne, with no uncommon nauseating, depressing, or disagreeable effects of the drug.

I therefore recommend the preparation of a fluid for hypodermic injections according to the following formula: Morphiæ acet. vel sulph. gr. xvj; acid. acetici (No. 8), gtt. ij; acid. salicylic. gr. iss; aq. destillat. f℥j. If a sediment is left undissolved, this liquid should be filtered, or, after standing a few days in a vial, or preferably a conical glass, the clear fluid may be drawn off by means of the hypodermic syringe itself, and preserved for use. By employing such a preparation, the practitioner is almost certain to avoid the disappointment in the relief of pain liable to arise from injecting a solution, the strength of which has deteriorated, and he will also escape that danger of producing abscess by the insertion of fungous elements beneath the integument, against which we have been cautioned by some authorities, although perhaps without sufficient cause for the warning.

In conclusion, I would suggest that a similar application of salicylic acid to the preservation of watery preparations of quinia, atropia, etc., to solutions of bromide of potassium, citrate of potassium, etc., and to vegetable infusions, when it is desirable to avoid the employment of even small quantities of alcohol, may prove of great value to the pharmaceutist as well as to the physician.

Discussion on Dr. Richardson's Paper.

After the reading of the preceding paper, the President, Dr. John C. Dalton, of New York, said:—Dr. Richardson has referred to two disadvantages that might result in the hypodermic use of solutions of morphia without this precaution, but in language which leads us to suspect that perhaps he does not think much of the danger of producing an abscess. I would like to inquire whether there is any definite information in regard to the danger, or whether in his opinion the danger exists at all?

Dr. Richardson said:—Theoretically I have felt inclined to suppose that danger would exist, but in order to test the theory I have tried several experiments, injecting my own arm with a solution containing fungi, and in no case has an abscess been produced.

Dr. Dalton said:—Of course it would be more agreeable to inject a fluid not containing fungous growths; at the same time ought we to anticipate that these growths would continue their development in a subcutaneous tissue? My attention was once very directly called to the difficulty that might arise from such development. I made a series of observations in order to determine how many definite kinds of microscopic fungi might be derived from ordinary atmosphere. Taking fresh slices of boiled potato, I placed them on a plate that had been immersed in boiling water, and covered them with a bell-glass, under which also a moist sponge was placed. A considerable variety of these microscopic growths showed themselves from time to time, of various colors; and notwithstanding their minute size and apparent want of specific character, they had differences in form and size and structure. A few weeks after finishing the experiment, I found one day on the back of my hand a spot which was irritable and itching; this spread, two or three other spots appearing, until finally I was compelled to give attention to the matter, and on examination I found that my hand was the seat of a tricophyton, which was finally removed after treatment for four or five weeks. It then occurred to me that perhaps I had inoculated myself while engaged in the experiments. I had been raising microscopic fungi, and I had unknown to myself been infected with them. Further, upon the same subject, Dr. Vandoren told me that in a series of experiments he had demonstrated that the ovum of the mosquito is not deposited directly in the water, but floats in the atmosphere, and is brought down by the rain. So it would seem that in reality there are a larger number of germs, both vegetable and animal, that may arrive at their destinations through the elements. My impression is that this fact in regard to the ovum of the mosquito is new.

Dr. Richardson said:—My recollection is that our natural histories gave us pictures of the mosquito in the act of laying eggs in the form of a boat which floated upon the surface of the water for some days or weeks before hatching. I think the experiments mentioned are entirely novel.

Dr. Dalton said:—In regard to the boat in which the eggs are contained, is it barely possible that Dr. Richardson may be thinking of the mosquito itself coming out from the integument of the larva?

Dr. Richardson said:—No, sir; that is a subsequent performance. But I wish to ask Prof. Dalton in respect to the infection of which he spoke, whether his health had been deteriorated in any way? I make this inquiry because one of the most difficult questions in regard to the development of these entophytic and epiphytic diseases is whether the health is first deteriorated, so that a suitable *nidus* for the fungi to grow in is afforded, or whether, on the contrary, the fungi are the primarily active agents which deteriorate the health.

Dr. Dalton said:—I can testify, with the greatest confidence, that I was in perfect health.

Dr. Richardson said:—Some years ago I had an interesting case bearing upon this point in my own family. On the chin of my little daughter appeared

a small pimple, which became inflamed, and seemed to have a yellow head upon it. In examining it I was struck with its remarkably dry appearance, and its sulphur-yellow rather than brownish hue. I placed a portion of it under the microscope, recognized the presence of the fungus of Favus, and soon cured the disease with corrosive sublimate solution. The child was in perfect health, and I could only account for the attack by supposing that she had leaned her chin on the sill of a car-window, where some person infected with achorion Schonleinii had accidentally left a few spores of the disease. I would like to ask another question, whether there has been any corroboration or disproof of the experiments described by Simon in regard to the dependence of ocular diphtheria upon micrococci developing in the cornea of rabbits; where two punctures were made, in the one side with a diptherized needle, and in the other side with a clean needle, in every case the result having been that the cornea infected was marked with brownish streaks, which under the microscope displayed minute fungus spores. I look upon it as exceedingly important to know whether the fungi can develop in an internal portion of the system, secluded from the air, and that in a previously healthy part of the organism.

Dr. DALTON said:—I am not familiar with any corroboration of those experiments. I tried some experiments of a similar kind, two or three years ago, with results which convinced me that it did not require for such parasitic growths the previous existence of a morbid condition of the recipient. The experiments were with regard to the ordinary decomposition or rotting of fruit. It can no longer be maintained that rotting is a continuation of the ripening process. An external wound is absolutely necessary to the rotting of any fruit with a hard integument, such as the apple and the pear, though it is not absolutely necessary with other fruit, like the orange. I tried the experiments with apples, and proved that they could be kept for any length of time, if uninjured, and also that rotting was contagious. The rot could plainly be seen to spread away from the point of contamination. I have exposed a dozen apples, half sound and half broken, to the ordinary atmosphere, and the rot always began at the point of injury. The spores came in from the atmosphere. Indeed, an injured apple can be kept from rotting by being protected from the atmosphere. I have taken a sound apple, and made a little cut in it, and then put it under a bell-glass, and kept it an indefinite time. The experiments can be easily tried, and are most convincing.

Dr. RICHARDSON said:—You speak about the rot starting from the wound in the integuments of the apple in a way that resembled the spread of erysipelas from the edges of a wound in the human body. Did it ever occur to you to cover the wound in the apple with carbolized putty before exposing it to the infection of the fungi which cause decay, and thus throw a ray of light upon one of the great surgical problems of the day?

Dr. DALTON said:—I never did so, but I think that it might be an interesting experiment.

Dr. RICHARDSON said:—I would ask Prof. Rudnew whether these experiments of Oertel and Nassiloff (the latter, I believe, a Russian observer), narrated in Prof. Simon's report, have been confirmed or disproved by others of his countrymen?

Prof. RUDNEW, of St. Petersburg, said:—I have studied these investigations, but have made no similar researches myself, and believe that the views of those gentlemen are still considered *sub judice*.

DISCUSSION ON DR. CHRISTOPHER JOHNSTON'S PAPER ON THE MICROSCOPY OF THE BLOOD.

After the reading of Dr. Johnston's paper, Dr. J. G. RICHARDSON, of Philadelphia, said:—I should like to offer an explanation in reference to my testimony at the trial in Herkimer County, New York. I did not state absolutely that the corpuscles were those of human blood, but that they *corresponded* to those of human blood. Microscopy has long been employed as an aid to the administration of justice; and serves easily, for example, to distinguish human blood from that of a fish, because the corpuscles in the former are round, while in the blood of the fish they are oval. At first the legal authorities demanded no more than this, but when the facilities for microscopic examination became more complete, we began to draw a still sharper line of distinction—that is, one between human blood and that of the musk-deer or goat. Now, with improved immersion lenses, we are, I contend, able to distinguish between the blood of a human being and that of an ox, horse, or other animal having corpuscles of similar size; but when circumstances do not thus narrow down the demands of justice in a trial, I would never attempt to discriminate the kind of blood with certainty. Our power to aid justice in this matter is due to the fact that when a man is arrested with blood-stains on him, and tries to explain how they got there, he generally alleges that he has been in a position to be stained by the blood of some animal; and then, by microscopic examination, we can distinguish between human blood and that of the ox, pig, or sheep, to which the suspicious stains are usually attributed.

Dr. JOHNSTON said:—That would not be a positive recognition of human blood-disks, which is what the courts desire; for the blood might be that of a dog or guinea-pig, and not of a human being.

Dr. HENRY D. DIDAMA, of Syracuse, N. Y., said:—I know of a case in which the question presented was, whether the blood was that of an ox or human being; and though, in such a case, an expert might not be able to say that the blood was human, yet he could prove that the statement made by the criminal was untrue. I wish to ask Dr. Johnston whether, if he should find a blood-disk $\frac{1}{3200}$ of an inch in diameter, he would be willing to swear that it was not the blood of an ox or pig? because, as I understand the matter, the blood-globules of the ox and pig never reach that size.

Dr. JOHNSTON said:—Where the variations were not exceedingly great, I would be unwilling to give an opinion.

Dr. RICHARDSON said:—I understand Prof. Johnston to say that, on examining some unlabelled slides of man's, dog's, and guinea-pig's blood, offered him by Dr. J. J. Woodward, he found himself unable to discriminate between them. This is what I should expect; but I would like to ask Prof. Johnston whether, if a person of unproved veracity should bring him a specimen of blood, covering the name, and telling him that it was from a sheep, and he should find, on measurement, that the corpuscles averaged $\frac{1}{3200}$ of an inch in diameter, he would not feel justified in contradicting the statement?

Dr. DIDAMA said:—Would not Prof. Johnston, if he found blood-disks of $\frac{1}{3200}$ of an inch, be certain that they could not have circulated in the capillaries of a sheep?

Dr. JOHNSTON said:—It is a very difficult question to answer, as both vessels and corpuscles are extremely elastic, and capillaries constantly allow corpus-

cles to pass through them, which are larger in diameter than the capillaries themselves.

Dr. JAMES TYSON, of Philadelphia, said:—It seems to me that this is an ambiguous mode of putting the question, because, as Dr. Johnston says, even if we could assert that a particular blood was not that of a sheep, we could not say that the corpuscles could not have circulated in the capillaries of a sheep, on account of the property of elasticity correctly attributed by Dr. Johnston to both corpuscles and capillaries, to say nothing of the varying size of the latter. But the fact is that the peculiar organization of the human mind has something to do with the drawing of conclusions. Some persons would feel at liberty to draw the same conclusions from the premises named by Drs. Didama and Richardson as they, while others would not. I, for example, would be willing to say that such blood was *more likely* to be that of an ox or sheep than that of a man, while I might not be willing to say absolutely "this is the blood of an ox or sheep," and not that of a man.

Dr. S. E. CHAILLÉ, of New Orleans, said:—I desire to ask two questions: I think we all agree with Prof. Johnston that human blood corpuscles cannot be positively distinguished from all others; but frequently, in court, some witnesses assert that a particular stain is human blood, while others say, no, it is the blood of an ox. The Court asks the microscopist, "Can you decide whether this is human blood or that of an ox—or, let us say, of a sheep?" Is it Prof. Johnston's opinion that such a decision could be made, and would he, under such restricted circumstances, feel justified in saying whether the blood was that of a sheep or of a man?

Dr. JOHNSTON said:—I could answer negatively, that the blood was not human.

Dr. CHAILLÉ said:—My second question is this: I have been told that certain specimens of blood have been offered to Dr. Richardson, and that he has been able to discriminate between them. I would ask of Dr. Richardson if such is the fact?

Dr. RICHARDSON said:—Such was the case, not in one series of specimens only, but in two.[1] The number of samples in each series was three; one being the blood of an ox, one that of a sheep, and the other human blood. I was able to distinguish between them by microscopical examination alone.

Dr. JOHNSTON said:—There is more than the mere diameter of the corpuscles to be considered; we must consider the *cachet*, or the stamp of individuality of the blood.

Dr. L. S. JOYNES, of Richmond, Va., said:—I would like to ask Dr. Richardson as to the relative ease of distinguishing between different bloods when dry and wet. Can we restore dried corpuscles so certainly as to distinguish whether they are human or otherwise? It is difficult to know how far blood corpuscles on the clothing are altered from their original condition.

Dr. RICHARDSON said:—My experience has been that in dry blood-stains there is a shrinkage of from five to ten per cent. That is, that the fresh blood corpuscles of man average $\frac{1}{3200}$ of an inch, while in stains they measure from $\frac{1}{3400}$ to $\frac{1}{3700}$. The blood corpuscle of an ox, which averages $\frac{1}{4267}$ of an inch, when fresh, would measure $\frac{1}{4600}$ or $\frac{1}{4700}$ after re-moistening.

Upon the conclusion of the discussion, Dr. RICHARDSON said:—As strong evidence of the presence of a true cell-wall in red blood corpuscles, upon the existence of which the value of my method for the diagnosis of blood-stains largely depends, I invite the members of the Section to inspect, beneath a Holmes's class microscope, a red disk of the Amphiuma tridactylum, in which the imperfectly crystallized cell-contents occupy the upper end, while the oval granular nucleus fills the inferior extremity, leaving the membranous capsule

[1] See American Journal of the Medical Sciences, July, 1874; also, London Monthly Microscopical Journal, Sept. 1874.

relaxed and wrinkled longitudinally, hanging like part of a half-flaccid balloon between them. (Fig. 1.) I also show, as corroborative testimony, a slide

Fig. 1 (× 400).

Fig. 2 (× 400).

bearing a blood corpuscle of the Menobranchus, which displays, within what I deem to be its limiting membrane, a single crystal made up of all the cell-contents except the nucleus.[1] (Fig. 2.)

[1] See Trans. Am. Med. Association, vol. xxi., 1870, p. 271.